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Single-Laser Approach for Fluorescence Guidance of Excimer Laser Angioplasty at 308 nm: Evaluation In Vitro and During Coronary Angioplasty

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Background and Objective: **Spectroscopic guidance of laser angioplasty has been attempted using a diagnostic He-Cd laser in addition to the therapeutic laser system. This study evaluated a single-laser approach for simultaneous ablation and fluorescence excitation.**
Study Design/Materials and Methods: **A spectroscopy system was coupled to a clinical XeCl excimer laser. Ablation of 162 human aortic samples in saline and blood with 45 mJ/mm^2 per pulse yielded 676 fluorescence spectra validated histologically. The same equipment was used in 16 patients for angioplasty of 18 coronary stenoses applying 500 to 1,725 pulses with 45 to 60 mJ/mm^2 under saline flushing. A total of 783 spectra were recorded and validated by intracoronary ultrasound (categories: atheroma, fibrous plaque, calcified lesion).**
Results: **In vitro, 5 types of spectra could be differentiated: (1) atheroma, (2) fibrous plaque, (3) calcified lesion in saline, (4) media, and (5) calcified lesion in blood. Discriminant analysis prospectively classified 576 validation spectra with the following sensitivity and specificity for each type: (1) 83.5 and 97.1%, (2) 85.7 and 96.8%, (3) 100 and 98.5%, (4) 98.1 and 99.3%, (5) 98.9 and 100%, respectively. In vivo, type 1, 2, 3, and 5 spectra were also observed, but not the media spectrum. The predominant sonographic category also prevailed in spectroscopy. Calcified lesions yielded type 3 and 5 as well as mixed spectra.**
Conclusions: **Using an excimer laser for angioplasty allows combining ablation and fluorescence excitation without a diagnostic laser. Principal types of atherosclerotic lesions and the media can be differentiated spectroscopically with this approach. Lasers Surg. Med. 20:382–393, 1997.** **© 1997 Wiley-Liss, Inc.**

Key words: atherosclerosis; excimer laser; fluorescence spectroscopy; laser angioplasty

INTRODUCTION

Recent multicenter trials demonstrated that excimer laser coronary angioplasty can be a useful adjunct to balloon angioplasty [1,2] especially in AHA/ACC type B2 and C lesions [3,4]. However, further technological improvements have to be made to optimize luminal gain and minimize the rate of dissections (13.0 to 14.7%) and coronary perforations (1.0 to 1.9%) [1,2]. A major step

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in this direction will be the development of a guiding system for laser angioplasty. Spectral analysis of laser-induced fluorescence is under investigation for this purpose.

Most data on arterial fluorescence have been accumulated using a low-power He-Cd laser (325 nm) for fluorescence excitation [5–10]. A double-laser system consisting of a dye laser operating at 480 nm for ablation and a diagnostic He-Cd laser was used in humans with obstructive peripheral artery disease [11–14]. However, perforation of the vessel wall was still observed in 12% [13] to 19% [14] of the lesions treated with this system despite spectroscopic guidance.

The advent of the XeCl excimer laser (308 nm) in angioplasty has the potential to combine tissue ablation and fluorescence excitation without the use of a diagnostic laser. Arterial fluorescence following excimer laser excitation has been studied in an air environment [15,16]. In the present study, a spectroscopy system was developed and coupled to a clinically approved XeCl excimer laser. This equipment was used to determine experimentally whether fluorescence spectroscopy with a single-laser approach could also be performed in saline and blood. Subsequently the feasibility of the method was to be demonstrated during excimer laser coronary angioplasty.

MATERIALS AND METHODS

Spectroscopy System

Tissue ablation was performed using a XeCl excimer laser approved for clinical angioplasty (CVX-300™, Spectranetics, Colorado Springs, CO). The fluorescence radiation emanating retrogradely from the catheter was coupled with a biconvex lens (focal length 100 mm) behind a dielectric mirror outside the "therapeutic" path of rays into a 2 m silica fiber with 600 μm core diameter ending at the entrance slit of a spectrograph (Fig. 1). This device was equipped with an optic grating exhibiting 405 lines/mm and a blaze wavelength of 450 nm (CP 140, Jobin Yvon, Lonjumeau, France). The interesting part of the diffraction spectrum (beside the 308 nm peak) was projected onto the photocathode of an image intensifier with a microchannel plate (PCO XX 1450 CK, AEG, Ulm, Germany). The highly intensified spectrum was imaged via a 2:1 taper (FP-87-1B, Schott Glaswerke, Mainz, Germany), onto a charged coupled device array with high blue sensitivity consisting of 604 × 576 pixels (NXA1011

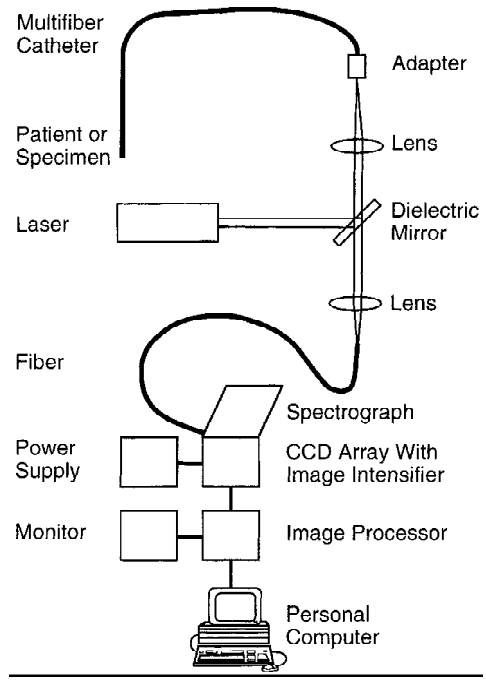


Fig. 1. Diagram of the experimental setup. The dielectric mirror is highly reflexive at 308 nm for the laser emission and transmissible for fluorescence radiation retrogradely emanating from the laser catheter.

Frame Transfer Sensor, Philips, Eindhoven, The Netherlands). The CCIR standard video output signal was directed to a control monitor and an image processor board (PCVISIONplus® Frame Grabber, Imaging Technology, Bedford, MA) on a personal computer with a 80386/33 MHz cache processor and coprocessor. The video signal was digitized with an 8 bit pixel depth and the sum profile over 100 of the 512 frame lines stored on hard disk. The spectrograph was triggered from the thyratron laser control unit without measurable time delay to the laser pulse. Each spectrum was recorded within 20 ms on a single-shot basis. Data acquisition and image processing was guided by prototype software. The spectral resolution of the system was 1.3 nm. The system was calibrated with a mercury vapor lamp. The spectral response curve (Fig. 2) was determined using a NBS 200 W iodide tungsten filament lamp standard (220C, Optronic Laboratories, Orlando, FL).

In Vitro Measurements

A total of 162 aortic specimens measuring 40 mm × 40 mm were obtained from 31 patients of either sex aged 34 to 91 years (median, 67 years) at necropsy 12 to 24 h postmortem. The samples were thoroughly rinsed in saline to avoid an in-

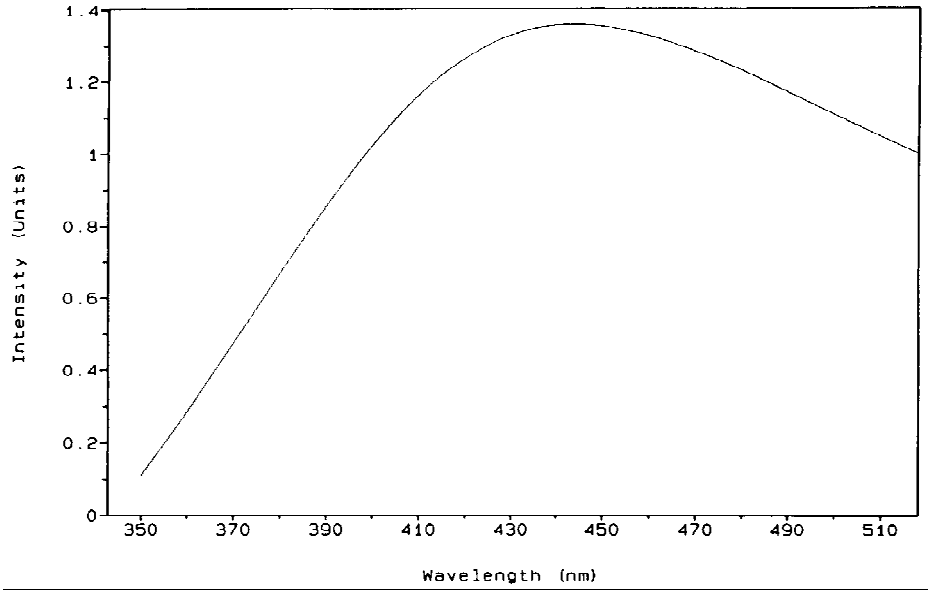


Fig. 2. Spectral response curve of the spectroscopy system. Note the high sensitivity in the blue spectral range.

fluence of oxyhemoglobin on the measurements [17,18], snap frozen in liquid nitrogen at −196°C and stored at −70°C until use. For the experiments, the arterial specimens were placed on a Petri dish filled with saline or heparinized blood. A commercial 2 mm multifiber coronary catheter (Extreme Vitesse™ C, Spectranectics) was positioned perpendicularly to the specimens with gentle pressure on a macroscopically selected site. Pulse energy was adjusted to 32 mJ (fluence 45 mJ/mm^2). Two to five pulses were required to ablate the normal intimal surface over the media, the intima of atheromas and fibrous plaques or the surface of calcified lesions. Thereafter, nearly identical spectra were reproduced with ongoing tissue ablation. At each measurement site, the spectrum following three nearly identical spectra and a background spectrum was stored for further evaluation. The site of laser irradiation was excised, fixed in 4% formalin, and processed for histological examination.

Quantitative Spectral Analysis

For quantitative analysis, the spectra were divided by the spectral response curve (Fig. 2). Fluorescence intensity at distinct wavelengths was then determined from each individual spectrum. Using a training set of randomly selected spectra, stepwise discriminant analysis with forward inclusion was performed (SPSS statistical program, SPSS, Chicago, IL) to choose intensity ratios as predictor variables which reduced Wilks' lambda [19] significantly. A P-value of 0.10 in the F-approximation was accepted as entry criterion. Fisher's linear discriminant functions [19] were deducted from the training set and then prospectively applied to the validation set of spectra to determine classification accuracy.

Histological Processing

Each spectrum corresponded to a histological section which was subjected to hematoxilin-eosin and Masson-Goldner trichrome staining. All sections were assigned one of four categories: normal; atheroma (Stary type III and IV lesion with multiple deposits of pooled extracellular lipid or lipid core [20]); fibrous plaque (Stary type V lesion with collagenous cap [20]); and calcified lesion.

Patient Characteristics

Sixteen patients with stable coronary heart disease and a hemodynamically effective stenosis of AHA/ACC type B2 or C morphology were included in the clinical part of this study. The protocol had been approved by the local ethical committee. Informed written consent was obtained from each patient. There were 14 men and two women aged 52 to 74 years (median, 64 years). Ten patients had prior myocardial infarction, six had undergone coronary bypass grafting. Ejection fraction ranged from 0.32 to 0.81 (mean ± SD, 0.62 ± 0.14). Two patients had angina of Canadian Cardiovascular Society class II, four patients of class III, and six patients of class IV [21].

Coronary Angioplasty and Spectroscopy

Excimer laser coronary angioplasty was performed with the same equipment used for the in vitro experiments. Pulses with an energy fluence between 45 and 60 mJ/mm^2 (13.4 to 42.2 mJ) were applied through 1.4, 1.7, and 2.0 mm multifiber catheters (Extreme Vitesse™ C and E) under saline flushing at a repetition rate of 25 Hz. Coronary percent diameter luminal stenosis was determined as the average of two orthogonal angiographic views using a quantitative analysis system (Digital Cardiac Imaging, Philips). The degrees of stenosis at baseline, after laser and percutaneous transluminal coronary angioplasty (PTCA) were compared with one-way ANOVA and two-tailed t-tests with Bonferroni correction.

Intracoronary Ultrasound

After passage with the laser catheter, intravascular ultrasound was performed by introducing a 3.5 F ultrasound catheter with a 30 MHz crystal (Sonicath™ CV, Boston Scientific, Watertown, MA) coupled to an ultrasound system with a frame frequency of 30 Hz (Intravascular Sonograph, Hewlett Packard Medical Products Group, Andover, MA). Atherosclerotic lesions were categorized into atheromas and fibrous plaques. The degree of calcification was quantified as an arc segment of the total vascular circumference. Percent area stenosis was determined with reference to the normal proximal coronary segment.

RESULTS

Histology

A total of 676 histological sections were prepared from the aortic specimens. Out of these, 179 were categorized as normal specimens, 117 as atheromas (Stary type III and IV lesion) (Fig. 3a,b), 153 as fibrous plaques (Stary type V lesion), and 227 as calcified lesions.

Training Set of Spectra

Among the corresponding 676 recorded autofluorescence spectra, five types could be differentiated:

Type 1: the spectrum of atheromas in saline (n = 74) or blood (n = 43).
Type 2: the spectrum of fibrous plaques in saline (n = 55) or blood (n = 98).
Type 3: the spectrum of calcified lesions in saline (n = 115).
Type 4: the spectrum of the media in saline (n = 90) or blood (n = 89).
Type 5: the spectrum of calcified lesions in blood (n = 112).

From each type of spectrum, 20 spectra were randomly selected for the training set. These spectra were normalized to their maximal peak and a mean spectrum ± SD in each pixel was generated. The spectrum of atheromas (type 1) showed a peak at 370 and 392 nm and a steep downslope to the right (Fig. 4a). The spectrum of fibrous plaques (type 2) showed the same primary shape as the spectrum of atheromas, but exhibited an additional peak at 450 nm and a minimum at 430 nm (Fig. 4b). The spectrum of calcified lesions in saline (type 3) was characterized by a tent-shaped curve with a single peak at 420 nm (Fig. 4c), whereas the spectrum of the media showed peaks at 370, 392, and 452 nm and a minimum at 430 nm (Fig. 4d). Finally, the spectrum of calcified lesions in blood (type 5) demonstrated a flat curve up to 430 nm with a steep upslope to a broad-based peak at 470 nm (Fig. 4e).

Spectral Classification

From each spectrum of the training set, fluorescence intensity I (λ) at λ = 392, 420, 430, 451 and 470 nm was determined as the arithmetic mean of 5 pixel contents (± 0,468 nm). Out of a variety of possible combinations, the two intensity ratios I(392 nm)/I(451 nm) and I(420nm)/I(470 nm) were selected as essential predictor variables using stepwise discriminant analysis with forward inclusion (Fig. 5). A final Wilks' lambda of 0.0237 was achieved. The following set of Fisher's linear discriminant functions f_1, f_2, . . . , f_5 was obtained from the training set (row 1 corresponds to spectrum type 1, row 2 to spectrum type 2 and so on):

$$\begin{pmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \\ f_5 \end{pmatrix} = \begin{pmatrix} 18.9539 & 41.5393 \\ 18.0943 & 20.6927 \\ -3.7308 & 49.1800 \\ 8.5323 & 21.0436 \\ 9.4898 & -1.2747 \end{pmatrix} \begin{pmatrix} \frac{I(392\text{ nm})}{I(451\text{ nm})} \\ \\ \frac{I(420\text{ nm})}{I(470\text{ nm})} \end{pmatrix} + \begin{pmatrix} -71.7954 \\ -34.1036 \\ -33.4355 \\ -16.8084 \\ -3.2557 \end{pmatrix}$$

These functions were applied equally weighted to the validation set of the 576 remaining spectra for prospective classification. As for the media (type 4), 156 out of 159 spectra were correctly classified yielding a sensitivity of 98.1%. Three spectra from fibrous plaques and one spectrum of a calcified lesion were incorrectly assigned to this type resulting in a specificity of

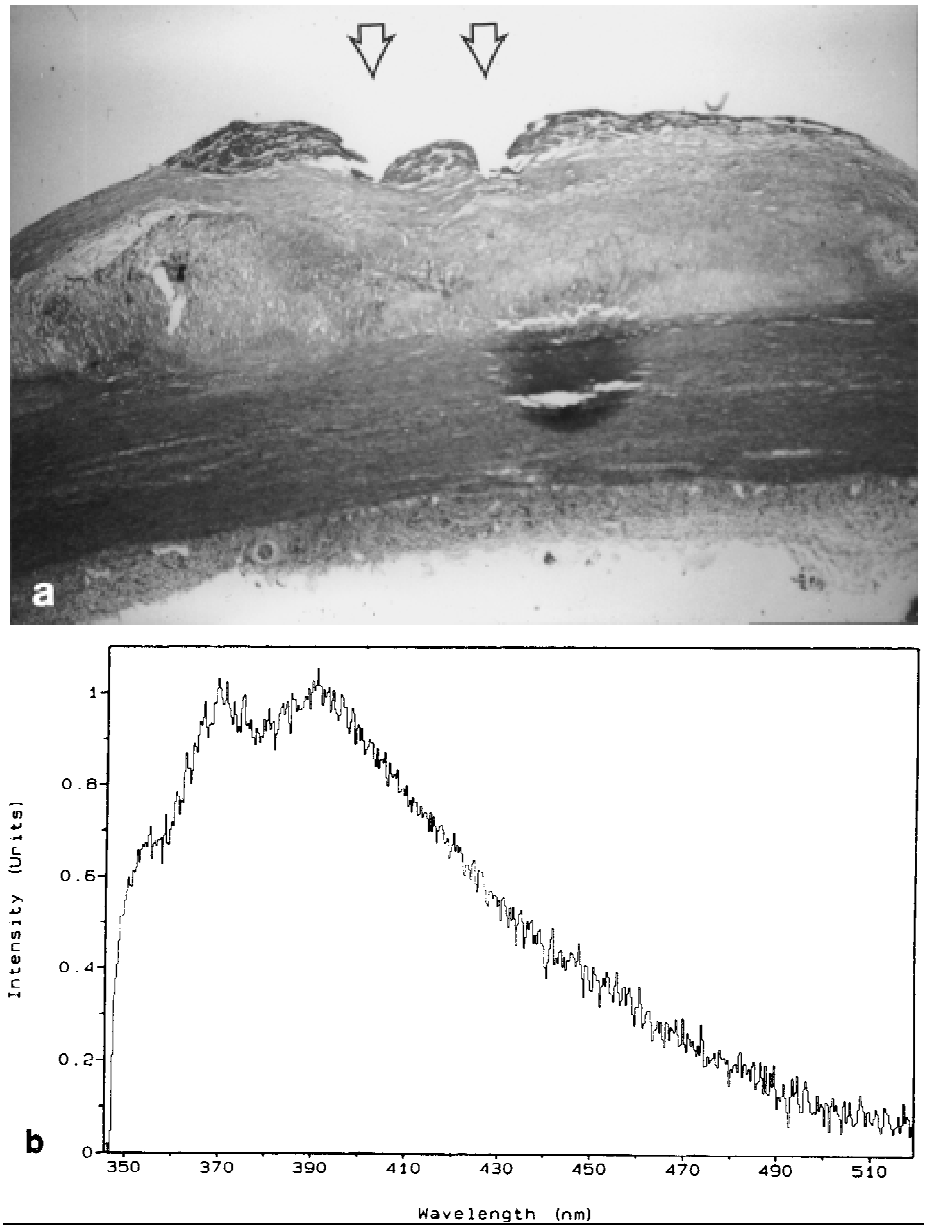
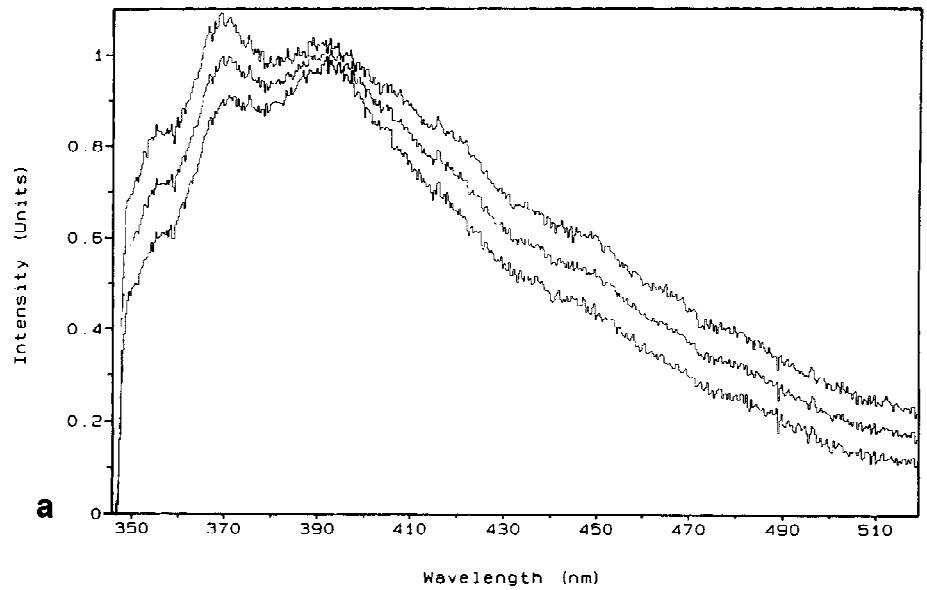


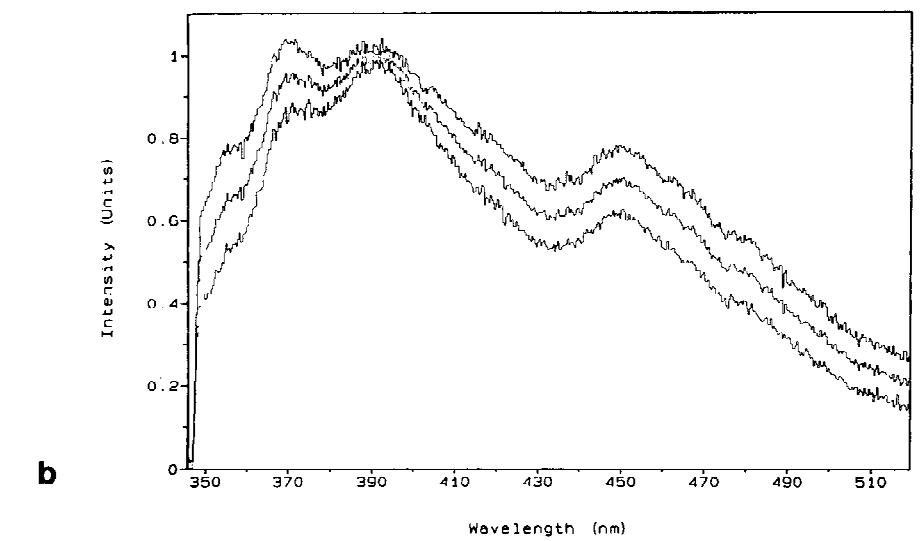
Fig. 3. Aortic atheroma. **a:** Histologic section showing an ablation crater (arrows) on top of the markedly thickened intima resulting from 12 pulses of 31.9 mJ from a XeCl excimer laser via a 2 mm multifiber catheter with central lumen. Hematoxilin-eosin stain, original magnification × 55. **b:** Fluorescence spectrum recorded with the last ablation pulse.

99.3% (Table 1). All 95 spectra of calcified lesions in saline (type 3) and 91 out of 92 spectra of calcified lesions in blood (type 5) were accurately classified with a sensitivity of 100 and 98.9% and a specificity of 98.5 and 100%, respectively. Eighty-one out of 97 spectra of atheromas (type 1) and 114 of 133 spectra of fibrous plaques (type 2) were correctly identified (sensitivity 83.5 and 85.7%, specificity 97.1 and 96.8%, respectively. All spectra were classified with a sensitivity of 93.2% and a specificity of 98.4% (Table 1).

Excimer Laser Coronary Angioplasty

Laser angioplasty was performed in 18 coronary lesions (right coronary artery 4 ×, left anterior descending 8 ×, left circumflex 1 ×, vein graft 5 ×) (Table 2, Fig. 6a). Between 500 and 1,725 pulses (mean, 865 ± 395) pulses were ap-





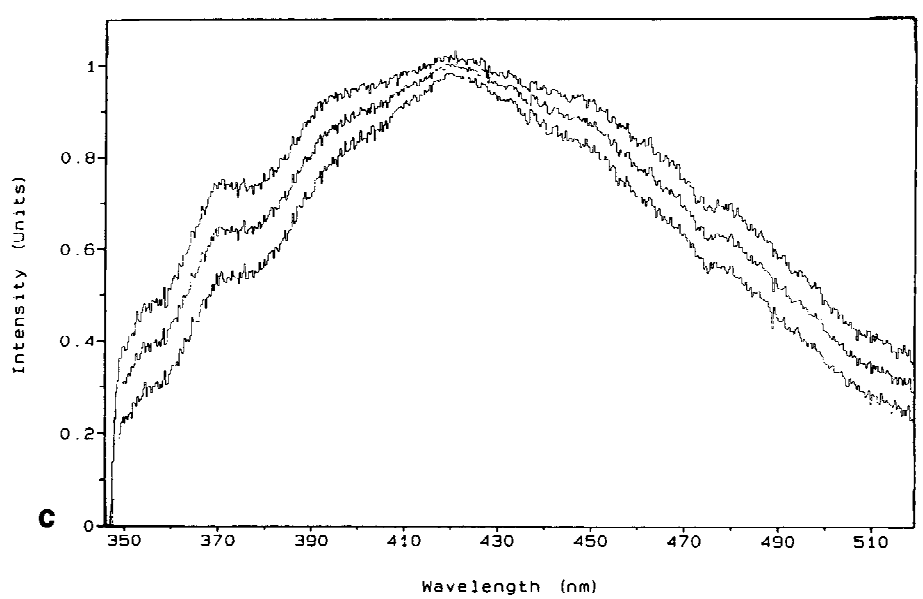


Fig. 4a–c. (continued on following page.)

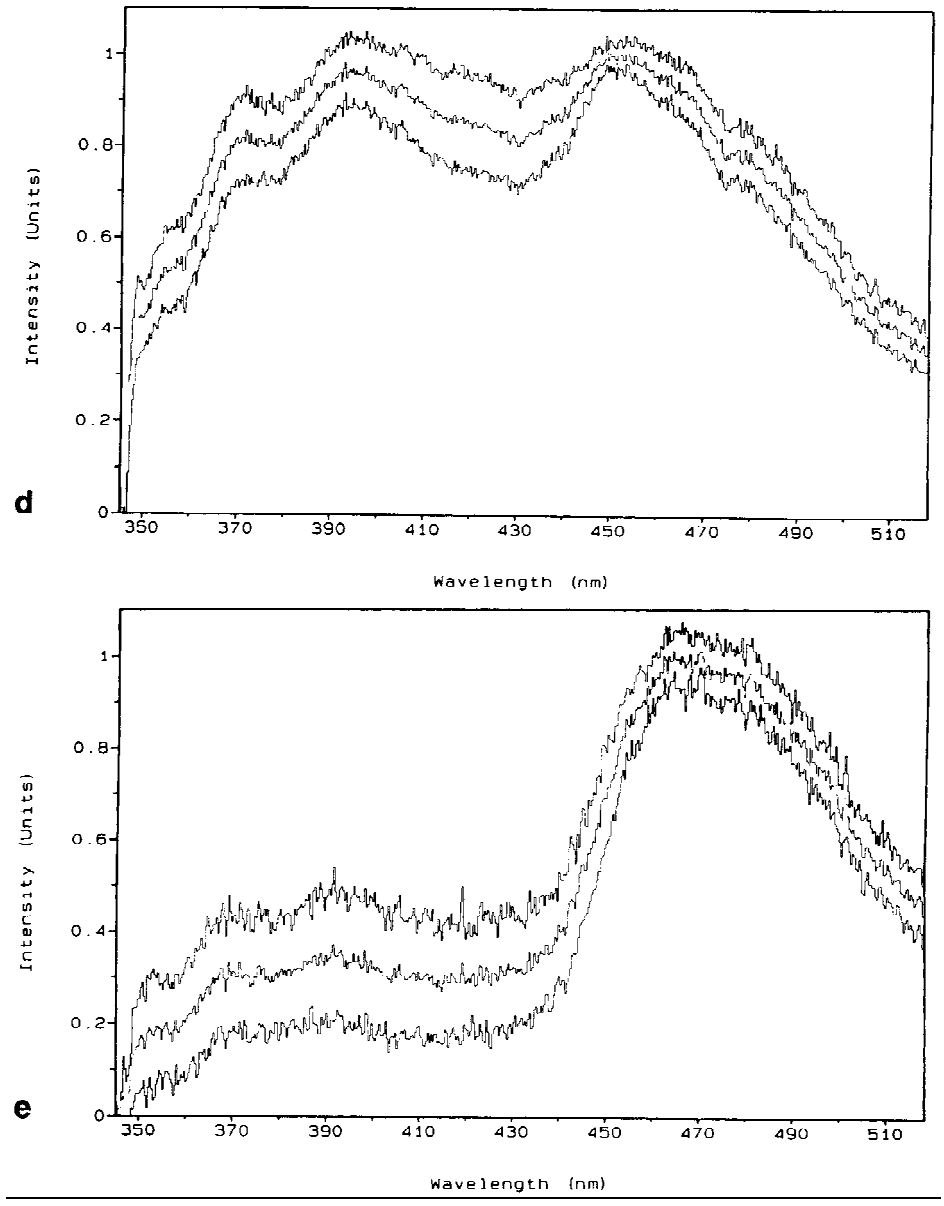


Fig. 4. Types of arterial fluorescence spectra observed after 308 nm excitation. Each plot represents the mean ± SD of the 20 randomly selected spectra of the training set characterizing each type of spectrum. **a:** Type 1, atheroma in saline and blood. **b:** Type 2, fibrous plaque in saline and blood. **c:** Type 3, calcified lesion in saline. **d:** Type 4, media in saline and blood. **e:** Type 5, calcified lesion in blood.

plied per stenosis. Laser angioplasty was followed by conventional PTCA in all lesions. There was an overall significant reduction in the angiographic degree of coronary stenosis by laser angioplasty and by PTCA ($P < 0.0001$). The degree of stenosis was significantly reduced by laser angioplasty at mean from 88 ± 11% to 59 ± 17% ($P < 0.0001$). In three lesions there was angiographic evidence of dissection after laser angioplasty with a flow preserved to at least TIMI grade 2 [22]. The final degree of stenosis after PTCA was 18 ± 19% ($P < 0.0001$ vs. baseline and post laser angioplasty). After PTCA there were five dissections, two of them required stenting (one of those emergency bypass grafting).

Intracoronary Spectroscopy

Due to the limited processing speed of the controlling personal computer, only every 16th spectrum could be both monitored and stored at a

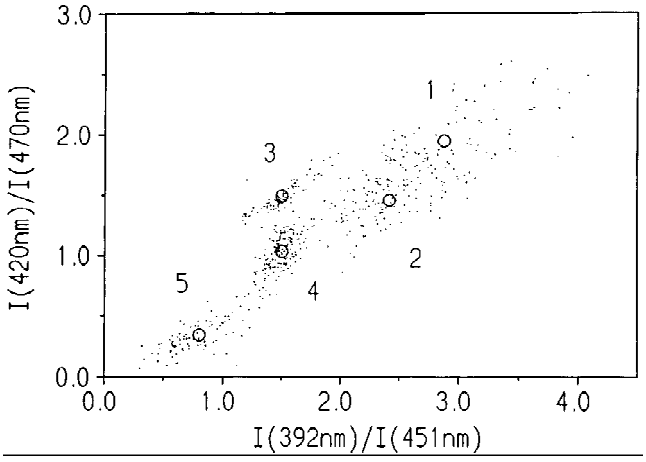


Fig. 5. Plot of the pairs of values assumed by the two intensity (I) ratios selected as predictor variables for discriminant analysis. Each point represents one of the 576 spectra of the validation set. The numbered open circles mark the group centroids for the corresponding types of spectra which are recognizable as clusters.

pulse repetition rate of 25 Hz during the clinical use of the laser. A total of 783 spectra were recorded. Due to a great variation in spectral intensity, the gain of the image intensifier repeatedly had to be adjusted manually. Whereas 1.7 and 2.0 mm multifiber catheters provided a sufficient signal-to-noise ratio, fluorescence intensity decreased markedly in patients with 1.4 mm catheters. Of the five types of spectra differentiated in vitro, four could be identified intracoronarily: the spectrum of atheromas (type 1), fibrous plaques (type 2), calcified lesions in saline (type 3), and calcified lesions in blood (type 5). The spectrum of the media (type 4) was not observed. Calcified lesions yielded type 3 and 5 (Fig. 6b) as well as mixed spectra. In each stenosis, the predominant type of spectrum corresponded to the predominant sonographic lesion category (Table 2). In two of the five vein graft stenoses (Patients 6 and 13) many spectra without notable fluorescence intensity above background were observed which originated from thrombotic material.

Intracoronary Ultrasound

In 14 of 16 patients, intravascular ultrasound was performed after laser angioplasty. In one patient with extensive dissection (Patient 12) and in another with insufficient luminal gain after laser angioplasty (Patient 13), the first ultrasound study was performed after PTCA and stenting. The degree of percent area stenosis was always higher than the degree of stenosis determined angiographically (mean, 67 ± 15%; P = 0.194). Nine of the 18 stenoses were calcified over 20° to 340° of the circumference (Table 2, Fig. 6c).

DISCUSSION

Spectral Analysis In Vitro

The normal and atherosclerotic arterial wall fluoresce predominantly in the blue and near ultraviolet spectral range necessitating short-wave excitation. For spectroscopic guidance of laser angioplasty, an additional He-Cd laser (325 nm) for fluorescence excitation has been incorporated in laser angioplasty systems [11–14]. Since excimer lasers per se are emitting ultraviolet pulses, increasing spread of the XeCl excimer laser for clinical angioplasty suggests combining laser ablation and fluorescence excitation. This would negate the need for a diagnostic laser and simplify fluorescence spectroscopy.

Laufer et al. applied KrFl excimer laser emission at 248 nm focused with a lens [15] and XeCl laser pulses at 308 nm above and below the ablation threshold through a 1,000 μm monofiber [16] to postmortem femoral artery segments. They demonstrated that arterial media, lipid plaques, and calcified lesions show characteristic fluorescence spectra following excimer laser excitation [15,16]. However, all these experiments were performed in room air. To evaluate the single-laser approach under conditions approximating more an in vivo setting and to extend our initial experience with an experimental laser system [23], the present study measured arterial fluorescence in a saline and blood environment using a clinical XeCl excimer laser and coronary multifiber catheters. Saline flushing is currently performed in many laboratories during coronary laser angioplasty to minimize photoacoustic damage to the vessel wall [24]. Moreover, this measure would also reduce potential interference of angiographic contrast medium with fluorescence excitation and detection [25]. Arterial media, fibrous plaques and atheromas showed each fluorescence spectra with typical line shapes. These spectra did not change between saline and blood and resembled noncorrected spectra obtained in air [15,16,23]. Calcified lesions, however, yielded markedly different fluorescence spectra in saline and blood. The different physical properties of these fluids may result in different photoproducts upon ablation and different absorption of fluorescence emission in the case of calcified lesions. The broad-banded spectra of calcified material in sa-

TABLE 1. Classification of the Spectra With Linear Discriminant Analysis

	Classification					Row total	Sensitivity (%)	Specificity (%)	Predictive value (%)	
Spectra	Type 1	Type 2	Type 3	Type 4	Type 5				Positive	Negative
Type 1	81	14	2	—	—	97	83.5	97.1	85.3	96.7
Type 2	14	114	2	3	—	133	85.7	96.8	89.1	95.8
Type 3	—	—	95	—	—	95	100	98.5	93.1	100
Type 4	—	—	3	156	—	159	98.1	99.3	97.5	99.3
Type 5	—	—	—	1	91	92	98.9	100	100	99.8
Total	95	128	102	160	91	576	93.2	98.3	93.2	98.3

TABLE 2. Parameters and Data of Fluorescence Spectroscopy During Excimer Laser Coronary Angioplasty*

Patient		Pr	EF	St	Tr	Lasr	Energy		Pulses	Angiography				Ultrasound				Spec
No.	Age (yr)/ gender	MI	(%)	Vs	Vs	cath (mm)	Selected (mJ/mm^2)	Measured (mJ)		Ty St	% Diam sten			% A St		Calc (degree)	Lesn Type	Prdm type
											At base	P LA	P PA	P LA	P PA			
1	74/F	—	81	2	RCA	1.7E	45	18.8	500	B2	66	22	0	29	—	0	FP	2
					RCA				644	C	100	55	0	63	—	0	A/FP	1,2
2	57/M	Ant	72	3	RCA	1.7E	45	18.4	746	B2	73	48	0	51	—	0	A	1
3	65/M	Ant	60	1	LAD	1.7	45	18.6	1,375	C	100	66	11	78	35	180	CL	5
4	52/M	Ant	65	1	LAD	1.7	45	18.8	875	C	100	68	26	64	32	150	CL	5
5	61/M	—	68	3	LAD	1.7	45	18.8	750	B2	92	56	12	68	—	0	A/FP	1,2
					LAD				625	C	72	53	10	60	—	30	FP/CL	2,5
6	62/M	Ant	45	1	SVG	2.0	45	32.0	600	C	84	42	28	50	—	0	FP	2
7	62/M	—	74	2	LAD	1.7	45	18.5	626	B2	82	35	10	57	37	40	FP/CL	2,3
8	54/M	Inf	58	3	LCx	1.4	45	13.4	750	B2	72	50	30	67	—	30	A/CL	1,5
9	57/M	Ant	81	1	LAD	1.7	45	18.8	1,048	B2	91	66	38	81	48	300	CL	3,5
10	67/M	—	63	3	SVG	1.7E	45/60	18.8/25.1	500	C	99	57	32	70	—	0	FP	2
11	63/M	—	32	2	SVG	1.7E	45	18.8	589	C	90	62	0	74	—	0	FP/A	2,1
12	69/M	—	75	1	LAD	1.7E	45/60	18.4/24.8	1,374	B2	92	92	76	—	81	340	CL	5
13	68/F	Inf	60	3	SVG	2.0	45	32.1	612	C	99	74	21	—	66	0	FP	2
14	71/M	Ant	60	2	LAD	1.4	45/60	13.6/18.2	1,735	B2	90	86	12	91	—	300	CL	5
15	70/M	Inf	38	2	RCA	2.0	45/60	31.2/42.2	589	B2	81	52	0	76	—	20	FP/CL	2,3
16	63/M	Ant	62	3	SVG	2.0	45/60/55	31.8/41.6/36.0	1,632	C	99	78	10	85	—	0	FP	2

*A = atheroma; Ant = anterior; A St = area stenosis; At base = at baseline; Calc = calcification; CL = calcified lesion; Diam sten = diameter stenosis; E = eccentric; EF = ejection fraction; F = female; FP = fibrous plaque; Inf = inferior; LAD = left anterior descending; Lasr cath = laser catheter; LCx = left circumflex; Lesn Type = lesion type; M = male; P LA = post laser angioplasty; P PA = post PTCA; Pr MI = prior myocardial infarction; Prdm type = predominant type of spectrum; RCA = right coronary artery; Spec = spectroscopy; St Vs = stenosed vessels; SVG = saphenous vein graft; Tr Vs, treated vessels; Ty St = type of stenosis.

line and blood also differed significantly from the corresponding spectrum in air dominated by calcium I and II lines [15,16,23,26]. This transition can be attributed to plasma formation in air which is not present in a fluid environment [23,26].

Prospective classification of fluorescence spectra was performed by Deckelbaum and his group using a low-power He-Cd laser for fluorescence excitation of aortic specimens in air [6,27,28]. Various classification algorithms (principal peak ratio, spectral width, multivariate linear regression, principal components analysis, decision plane analysis, Bayes decision theory, backpropagation networks) were evaluated [27, 28]. Principal components analysis using a training set of 100 and a validation set of 82 spectra yielded the best overall sensitivity of 96%, with a sensitivity of 95% for normal and of 98% for atherosclerotic specimens [27]. Only binary prospective classifications were investigated. The present study tried to differentiate between five types of fluorescence spectra: the spectrum of atheromas in saline and blood, fibrous plaques in saline and blood, calcified lesions in saline, arterial media in saline and blood, as well as calcified lesions in blood. Linear discriminant analysis yielded a sensitivity and specificity > 96% for the prospective spectroscopic classification of media, lipid plaques (atheromas plus fibrous plaques) and calcified le-

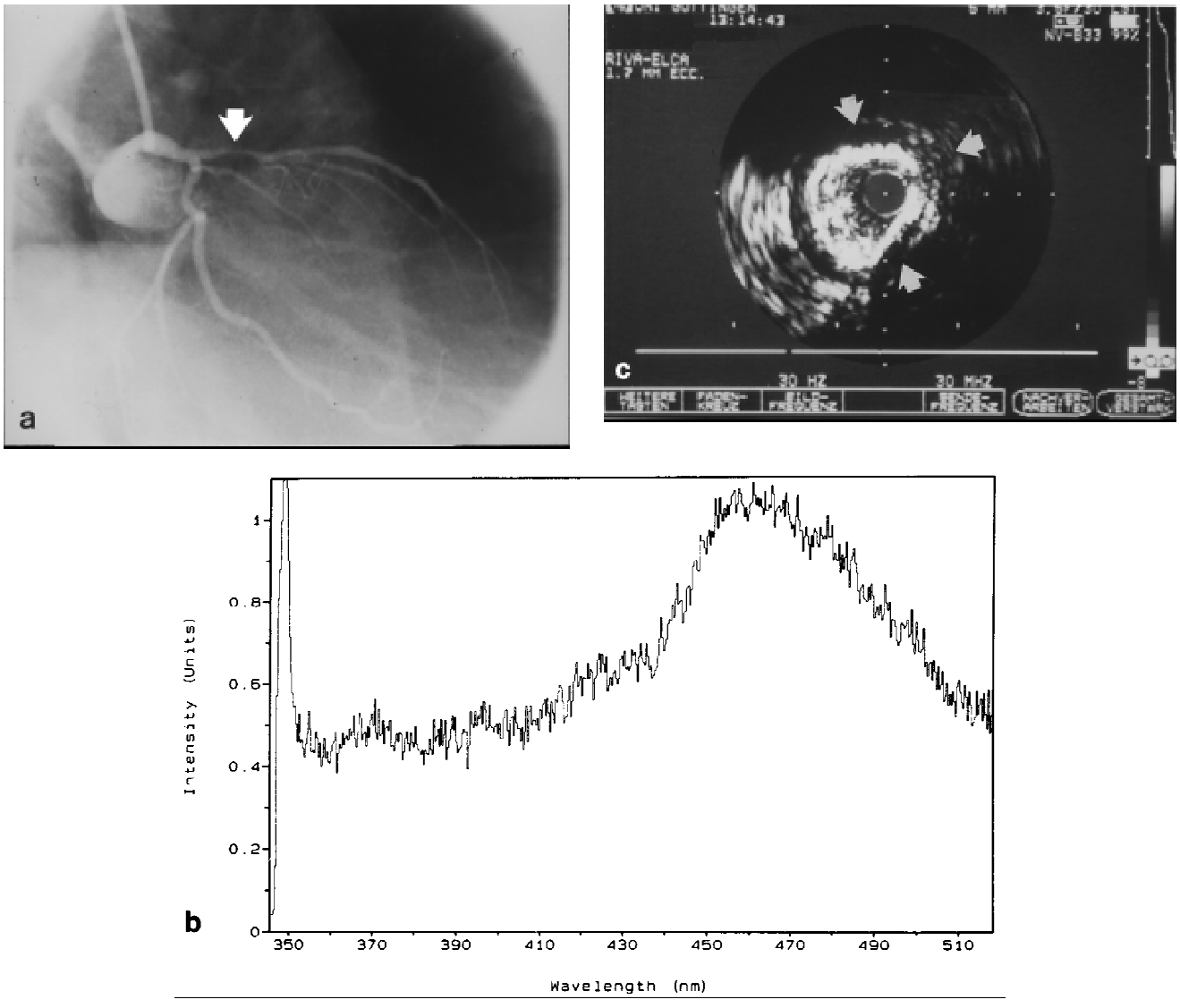


Fig. 6. Intracoronary fluorescence spectroscopy in a 57-year-old male with single-vessel disease (Patient 9). **a:** Right anterior oblique view of the left coronary artery showing a proximal 91% left anterior descending stenosis (arrow) prior to angioplasty. **b:** Representative fluorescence spectrum (type 5) obtained during excimer laser angioplasty of this lesion. **c:** Intracoronary ultrasound of the lesion after passage with the laser catheter showing calcification in about 300° of the luminal circumference (arrows).

sions in saline and blood. Lipid plaques could be further differentiated into atheromas and fibrous plaques with a sensitivity > 83% and a specificity > 96%. This differentiation may be important to risk stratification [29].

Intracoronary Fluorescence Spectroscopy

Bartorelli et al. recorded arterial fluorescence in vivo using a 200 μm core monofiber during open heart surgery, peripheral percutaneous transluminal angioplasty, and in eight patients with coronary occlusion prior to conventional wire recanalization [30]. They determined peak intensity, peak position, and shape of the spectral curve and tried to differentiate between normal sites, noncalcified plaques, and calcified lesions [30]. To our knowledge, the present study is the first to demonstrate the feasibility of the single-laser approach for fluorescence spectroscopy in humans during excimer laser coronary angioplasty. Except for the spectrum of the media, all types of spectra observed in vitro were also encountered in vivo. The fluorescence spectra were validated using intracoronary ultrasound. The tissue category predominating on spectroscopy also prevailed in ultrasound. Thrombotic mate-

rial could not be identified spectroscopically. Due to the limited processing speed of the personal computer controlling spectroscopy, only a fraction of the spectra excited in vivo could be monitored and stored. A faster computer system would diminish the loss of information. Image intensifier gain was manually adjusted in this study. This should be controlled automatically, since the spectral intensity varied markedly during intracoronary ablation.

Laser Angioplasty

In each patient, excimer laser coronary angioplasty was followed by conventional PTCA. The overall rate of additional PTCA after laser angioplasty was reported to be 71 to 79% [1,2]. However, in the largest excimer laser coronary angioplasty registry to date comprised of 3,000 patients, the rate of additional PTCA increased from 71% in the first 2,000 to 95% in the last 1,000 patients [2].

Intracoronary Ultrasound

While angiographically normal coronary segments showed a clear three-layer appearance, atherosclerotic intima could usually not be delineated accurately from the media. This has also been observed by other investigators [31,32]. The residual percent area stenosis on sonography after laser angioplasty as well as after PTCA was always higher than the corresponding percent diameter stenosis on angiography. This is in keeping with the results of a study on intravascular ultrasound after PTCA [33]. Most lesions revealed calcification on ultrasound imaging, agreeing with another investigation [34].

Study Limitations

A total of four categories of atherosclerotic lesions were studied in the present investigation. However, complex lesions such as ulcerated or hemorrhagic plaques were not evaluated. These lesions may provide mixed spectra which could be difficult to classify.

Slight variations in intracoronary position between the ultrasound and the laser catheter were unavoidable despite fluoroscopic control. Sonographic validation of the fluorescence spectra excited during ablation had to be performed after removal of a major part of the atherosclerotic lesion. These shortcomings resulted in uncertainties in ultrasound validation of the in vivo spectra.

Clinical Implications

This study demonstrates that ablation of atherosclerotic lesions and excitation of arterial fluorescence can be combined when using a XeCl excimer laser. This obviates a second low-power laser solely to induce diagnostic tissue fluorescence. Principal types of atherosclerotic lesions and arterial media can be accurately differentiated spectroscopically during experimental plaque ablation and coronary laser angioplasty with this approach. Distinct technical improvements are required prior to routine clinical application of the spectroscopy system described.

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